

Version 2.0



Abstract

Grant Number: 5F31NR007525-02

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PI Title:

Project Title: HYPOTHERMIC TREATMENT OF NEONATAL ASPHYXIC
BRAIN INJURY

Abstract: *Perinatal hypoxia-ischemia (HI) has potential lifelong consequences for infants and children including movement disorders, epilepsy, and developmental delay. Therapeutic and pharmacologic interventions are either unsuccessful or controversial, limiting treatment to supportive care. Hypothermia is a potential intervention suggested to provide protection in some newborn animal models of HI, however through unclear mechanisms. Its long-term protection is unknown. HI injury leads to brain damage through a variety of pathways, including excitotoxicity mediated via glutamate pathways, and energy failure. Therefore, the purpose of this study is to investigate in a clinically relevant animal model of HI, the effects of hypothermia related to 1) neuroprotection at 14-days 2) extra-cellular glutamate concentrations and glutamate transporters (GLT1, EAAC1), and 3) energy metabolism (glucose consumption and mitochondrial function). One-week old anesthetized piglets will be subjected to asphyxic cardiac arrest. After cardiopulmonary resuscitation animals will be randomly assigned to undergo mild hypothermia or normothermia for 24 hrs. Neuronal cell density will be counted at 14-days of survival. Microdialysate determination of extracellular glutamate concentrations, expression of glutamate reuptake transporters measured by western immunoblots and immunocytochemistry, autoradiographic determination of regional glucose consumption, and cytochrome oxidase histochemistry will be investigated during the transition from hypothermia to normothermia when cortical electrical activity emerges and when seizure activity often occurs. Neurological assessment will be performed daily. Through investigation of hypothermia in a clinically relevant animal model of HI, it is expected that the findings from this study will contribute to the understanding of potential mechanisms of*

protecting the human newborn from the sequelae of HI encephalopathy and for optimizing protocols for clinical implementation of hypothermia.

Thesaurus Terms:

*cerebral ischemia /hypoxia, heart arrest, hypoxia neonatorum, induced hypothermia, nervous system disorder therapy, nonhuman therapy evaluation
brain metabolism, corpus striatum, cytochrome oxidase, disease /disorder model, enzyme activity, glucose metabolism, glutamate, glutamate transporter, somesthetic sensory cortex autoradiography, electroencephalography, newborn animal, swine, western blotting*

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Fiscal Year: 2001

Department: NONE

Project Start: 22-MAY-2001

Project End:

ICD: NATIONAL INSTITUTE OF NURSING RESEARCH

IRG: NRRC

